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November 2, 1999

Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Services
United States Food & Drug Administration
Room 1061 (HFA-305)
5630 Fishers Lane
Rockville, MD 20852

Re: Guidance on Quality System Regulation Information
For Various Pre-Market Submissions
Draft Guidance – Not for Implementation
Draft released for comment on August 3, 1999

Ladies & Gentlemen,

Beckman Coulter appreciates the opportunity to comment on FDA's "Draft Guidance on Quality System Regulation Information for Various Pre-Market Submissions" as issued for comments on August 3, 1999. This letter provides summary comments regarding the proposal. Comments on specific aspects of the draft guidance are provided in the attached table.

Beckman Coulter is a major international manufacturer and worldwide distributor of medical and scientific test systems, including *in vitro* diagnostic test systems. The company was formed in October 1997 by the combination of what was then Beckman Instruments, Inc., based in Fullerton, California and Coulter Corporation, based in Miami, Florida. Beckman Coulter headquarters are located in Fullerton, California, with manufacturing facilities located in Fullerton, Brea, Carlsbad, and Palo Alto, California; Miami, Florida; and Galway, Ireland. The company's 1998 sales totaled \$1.7 billion.

Beckman Coulter has a number of general comments regarding the draft guidance, and is opposed to various changes proposed by this Draft Guidance. These comments may be summarized into the following categories:

The Guidance establishes new requirements

The draft guidance appears to be establishing new requirements for PMA submissions. Regulations published at 21 CFR 814.20 and other guidance provided by FDA Blue book

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memoranda such as "Refuse to File Checklist" clearly specify the information to be provided for submissions. The changes in the proposed Draft Guidance imply that the information required by established regulations is inadequate. However, prior to the issuance of this proposed guidance, Beckman Coulter is not aware of any communications by the FDA that inadequate information was provided in the many PMAs reviewed to date.

Some of these new requirements also appear to overlap with the already well-defined pre-approval inspection processes. It appears that in some instances, the ODE reviewer is not only performing the review to determine if the device is safe and effective, but is also performing portions of the pre-approval site inspection. It is not appropriate for ODE to undertake these reviews because ODE reviewers are not in a position to evaluate the efficiency of the manufacturer's systems.

The Guidance is not consistent with FDAMA and with the implementation of Design Control requirements:

The new draft Guidance does not pass the test of the FDAMA "least burdensome" concept. Adding significant items such as copies of the manufacturer's development strategy and its entire Quality Manual contradicts the spirit, if not the intent, of this requirement. New requirements, without concessions in other areas, are by nature an additional burden.

The Guidance requires that a copy of the company Quality System Regulation policy manual be submitted (pg. 8, Manufacturing Dossier, #1), and appears to require that a copy of the entire design control file be submitted (pg. 8, Manufacturing Dossier, #1). This is certainly not "least burdensome".

The regulations require the "use of design controls", but not their submission to FDA. The regulations in 21CFR 814.20(b)(4)(v) state that: "The methods used in, and the facilities and controls used for, the manufacture, processing, packing, storage and, where appropriate, installation of the device". This provides sufficient detail so that a person generally familiar with good manufacturing practice can make a knowledgeable judgment about the quality control used in the manufacture of the device.

The Guidance presents confidential information risks

The Guidance document requires a copy of the development plan (page 4 and continuing) including "information on the chronology of the development strategy". This requirement intrudes on areas outside of FDA's purview such as marketing inputs and other confidential business information. It is inappropriate for FDA to require this type of information. There is also the risk that the Manufacturer's design control and quality system, as well as the device development process, may be released to competitors through the FOIA.

The Guidance increases the level of documentation in the Submission

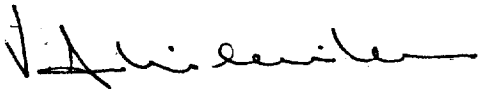
FDA is also asking for copies of all written procedures used in all phases of design control and review plus the validation plans/results. This requirement creates considerable additional documentation that the FDA has to review in its entirety, leading to longer review time, more questions, and increased times to market. The regulations require the "use of design controls", but not their submission to FDA. As mentioned above, the regulations in 21CFR 814.20(b)(4)(v) already require sufficient detail, and the new guidance would increase detail to the point of the absurd.

The Guidance increases potential for differing opinions

The level of detail required by this guidance increases the potential for "second guessing" by the Agency, as well as conflicts in interpretation between ODE and the field inspectors. For example, under the design validation section this guidance would require a summary of the completed risk/ hazard analysis. FDA may disagree with the risk analysis methods or with the manufacturer's conclusions, leading to lengthy discussions and/or possible refusal to approve. Similarly, an ODE reviewer working only with documents may find fault with a company's design control process, while a field inspector with more complete information may find them adequate. The premise of the QSR design control requirements was to establish a design control process. Including the complete design control and quality system detail in the required information puts more emphasis on the system than on the actual adequacy of the product.

Again, Beckman Coulter appreciates the opportunity to comment on this proposed guidance. Any questions regarding the comments provided in this letter or the attached table can be addressed to my attention at the letterhead address.

Sincerely,



Vlad Ghiulamila
Manager
Global Regulatory Compliance

RJO/VG:raf

Attachment: Table of Comments

**Specific Comments on Quality System Regulation
Information for Various Pre-market Submissions**

Draft Guidance – Not for Implementation
Released for Comment on August 3, 1999

SECTION	TEXT	COMMENT
Introduction (page 3, paragraph 2)	"PMA and PDP submissions should include a complete description of design controls and manufacturing information"	<ul style="list-style-type: none"> • The new Draft Guidance proposes that the complete design control information be included, rather than the current summary of design control. <i>A Manufacturers' design control system may be very extensive and complex. To include this information in a submission does not add any information that would assist the reviewer in determining whether a device is safe and effective.</i> • The new Draft Guidance would require all manufacturing information to be included in a submission, rather than the only the pertinent information, not only in a new PMA, but in modular PMAs, streamlined PMAs, and PMA supplements. <i>The current regulations require that enough information be submitted so that the reader may gain a general understanding of the data and information, such that a person generally familiar with current good manufacturing practice can make a knowledgeable judgment about the quality control used in the manufacture of the device (21 CFR 814.20(B)(4)(v))</i> • While not specifically stating so, the Draft Guidance would also be applied to programs which are specifically designed to decrease the level of documentation sent to FDA for supplements, such as the Express Supplement program, and the 30-day Notice program.

SECTION	TEXT	COMMENT
Introduction (page 3, paragraph 2) <i>Cont'd.</i>		<i>Adding the complete design control and manufacturing information to a supplement designed to decrease both the manufacturers and FDAs workload would negate any benefit from these programs.</i>
Information Requirements, Background (page 4, last paragraph)	"However, once a manufacturer decides to develop a design, the QS regulation requires the use of design controls to ensure that the design specification released to production meet the approved design requirements"	<p>This statement, by itself, is quite acceptable. Manufacturers do use design control to develop and manufacture products. However, the submission of a manufacturer's complete design control file assumes that their design control is not sufficient to satisfy FDA requirements.</p> <p>It will also lead to "second guessing" on the adequacy of the design control program, second guessing on the appropriateness of decisions made by the manufacturer, and second guessing on the marketing decisions of the manufacturer.</p>
Design Control Dossier (pages 4-8, all subheadings)	"A copy of the written procedures....."	<p>The submission of a manufacturer's complete design control procedure system is unnecessary. A reviewer is not in a position to interpret or analyze these procedures for adequacy; that is the purview of the field inspector. Including this information in a submission could be duplicative with the field inspection, increases the size of a submission unnecessarily, and increases review times. It is not needed, and may require the manufacturer to write a new submission or supplement if any revisions are made to either the design control or quality system.</p> <p>If copies of these procedures are required by the field inspector prior to the site inspection, it is more appropriate that the manufacturer be contacted at that time.</p>

SECTION	TEXT	COMMENT
Design Control Dossier (page 4, paragraph 3)	"The design and development plan or a summary of the plan"	<p>This section by itself is acceptable, provided that FDA agrees that a summary of either the Manufacturer's design control program itself, or a summary of the design control program as applied to the subject of the PMA, is sufficient.</p> <p>The manufacturer has no assurance that these documents, developed at the manufacturer's expense will remain confidential.</p>

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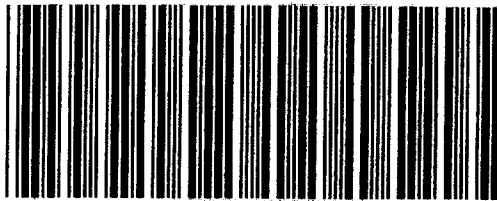
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